# Oxidation of Alkoxyphenols. Part 28.[1] On the Configuration of 2,2'-Diphenoquinones

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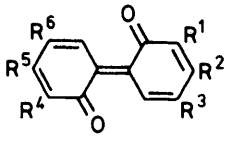
The n.m.r. spectra of a number of 2,2'-diphenoquinones imply that they have the *trans*-configuration. The importance of charge-separated structures in unsymmetrical quinones is discussed in relation to the formation of oxepino[2,3-*b*]benzofurans.

2,2'-Diphenoquinones (1), in comparison with their 4,4'-isomers, are relatively uncommon and of limited stability. Those with t-alkyl substitution at the 3- and 3'-positions have been shown to isomerize spontaneously in solution to oxepinobenzofurans (2),[2] previously described erroneously as benzoxets. We have recently shown that in contrast the unhindered diphenoquinone (1a) spontaneously trimerizes in solution,[3] and it is therefore of interest to determine the configuration of these quinones.

Unfortunately the very small crystal habit of those examples which have been crystallized precludes the use of *X*-ray crystallography. Those which are highly oxygenated and apparently more stable are also very insoluble, but by making use of F.T. n.m.r. spectroscopy we have been able to obtain the data shown in the Table. The unusually low-field chemical shift (δ 7.75—8.43) of one pair of ring protons in each quinone requires that the molecules have the *trans*-configuration, in order that the carbonyl groups may exert a deshielding effect not possible in the *cis*-configuration. This observation supports the intuitive assumption that the proximity of the carbonyl groups in the *cis*-configuration would produce excessive steric and dipolar interference.[4]

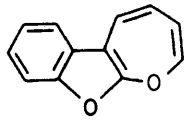
The chromophore in these quinones is closely related to that of indigo and thioindigo. Both these compounds have been shown to be more stable in the *trans*-configuration,[5,6] and their *cis–trans* isomerization is particularly facile.[7,8] Charge-separated structures such as (5) have been invoked [4,9,10] to account for the chemical reactivity of these quinones, and this type of polarization would clearly also facilitate geometrical interconversion. We have shown previously [11] that partial oxidation of biphenyl-2,2'-diols in neutral solution produces monophenoxy-radicals in which the unpaired electron is symmetrically shared by the two rings, which must therefore be held in a *cis*-configuration by a bridging hydrogen as shown in structure (3). Further oxidation is therefore likely to result initially in the formation of a *cis*-diphenoquinone: such a configuration is inconsistent with the n.m.r. data of the Table, and again points to the ease of interconversion of the *cis*- and *trans*-forms.

Experimental evidence for the importance of dipolar structures, not only in facilitating the rotation of 2,2'-diphenoquinones, but as intermediates in their isomerization to oxepinobenzofurans, comes from a comparison of the behaviour of the isomeric diols (4) and (5) on oxidation. In a previous paper [12] it was shown that oxidation of the diol (4) gave a blue solution that quickly faded and showed the n.m.r. spectrum of only the oxepinobenzofuran. The extreme instability of the intermediate diphenoquinone may be attributed to its lack of symmetry, which should result in a higher degree of polarization. If the equilibrium, established by Baltes and Volbert [4] for the diphenoquinone (1h), between diphenoquinone and oxepin is represented mechanistically as in the Scheme, one would predict that only one of the two possible oxepins would be obtained, that which would result from attack by the more negative of the two carbonyl oxygens. This was found to be the case, only compound (10) being detected, and none of the alternative (10a).

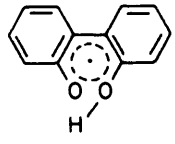


(1)

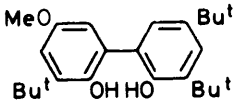
| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ |
|---|---|---|---|---|---|---|
| a; | H | Bu$^t$ | OMe | H | Bu$^t$ | OMe |
| b; | H | Bu$^t$ | $OCH_2Ph$ | H | Bu$^t$ | $OCH_2Ph$ |
| c; | H | OMe | OMe | H | OMe | OMe |
| d; | H | $-OCH_2O-$ | | H | $-OCH_2O-$ | |
| e; | Pr$^i$ | H | OMe | Pr$^i$ | H | OMe |
| f; | Bu$^t$ | H | Bu$^t$ | H | Bu$^t$ | OMe |
| g; | Bu$^t$ | H | Bu$^t$ | Bu$^t$ | H | Bu$^t$ |
| h; | Bu$^t$ | H | OMe | Bu$^t$ | H | OMe |



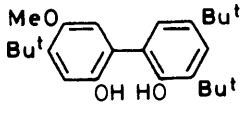
(2)



(3)



(4)

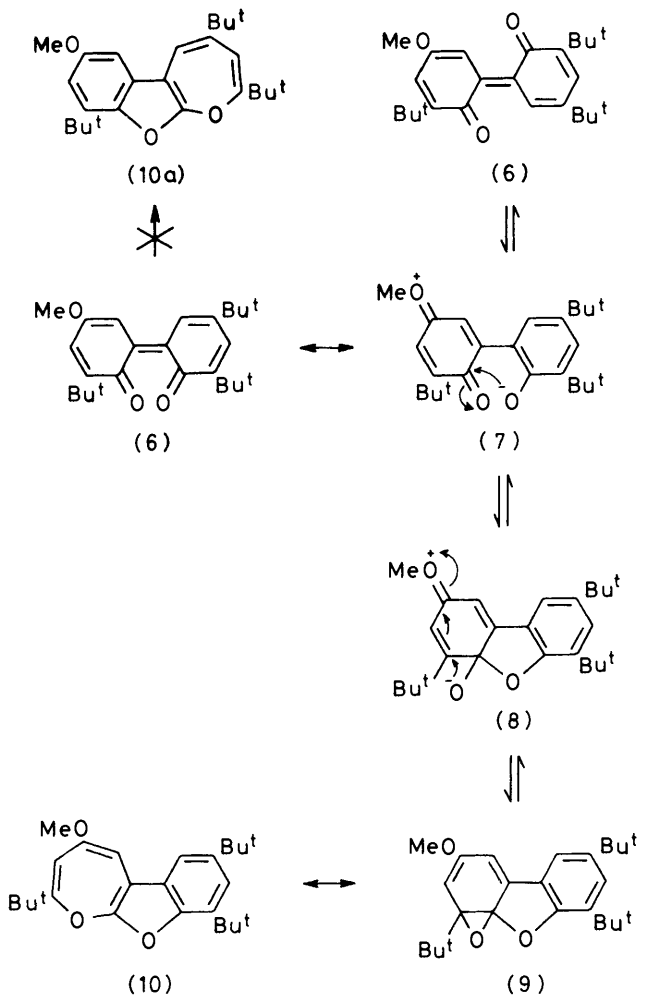


(5)

**Table.** N.m.r. chemical shifts (δ) for the ring protons of 2,2'-diphenoquinones (1a—h) in $CCl_4$ or $CDCl_3$

| Compound | δ (*J*/Hz) |
|---|---|
| (1a) | 8.26, 6.05 |
| (1b) | 8.43, 6.09 |
| (1c) | 8.26, 5.71 * |
| (1d) | 8.10, 5.88 * |
| (1e) | 8.14, 6.52 (2.8) |
| (1f) | 8.15, 6.06, 8.07, 6.92 (2.3) |
| (1g) | 7.75, 6.87 (2.3) |
| (1h) | 7.92, 6.59 (2.7) |

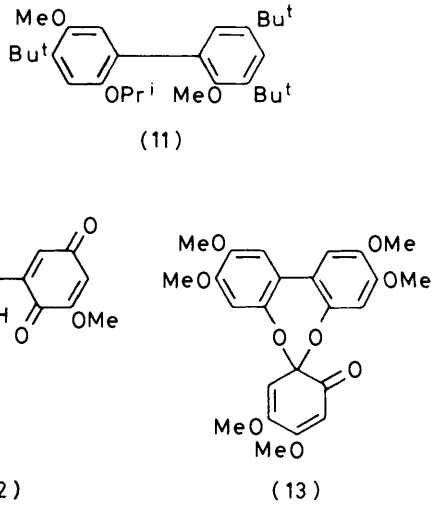
* $CDCl_3$ as solvent.




Scheme

By contrast, the isomeric diol (5) gives on oxidation a typically blue diphenoquinone (1f) of reasonable stability in dilute solution in non-polar solvents. This quinone shows no tendency to isomerize to an oxepin, so that in this case the equilibrium of the Scheme lies far to the left. The reason for this is suggested by the work of Hayes *et al.*[13] who have shown that the equilibrium between simple arene oxides and oxepins is favourable to the oxepin when a substituent is present at C-2, and they have explained this effect in terms of the hyperconjugative ability of a C-2 substituent in providing resonance stabilization for the oxepin. The reverse effect, *i.e.* stabilization of the oxide, was found when C-3 was substituted instead. These are just the differences in substitution patterns between the potential oxide/oxepin rings of the quinones (6) and (1f). Moreover, although nearly all the reactions of oxepino[2,3-*b*]benzofurans appear to involve the arene oxide isomer, there is evidence [2] that 2,2′-diphenoquinones do not exist to any appreciable extent in the oxide form, either in solution or in the solid. The fact that the diphenoquinone (1f) does not form an oxepin even though substitution at C-2 is available on one side of the molecule supports the intermediacy of the dipolar form (7), and a consequent nucleophilic attack, as in the Scheme, rather than an electrocyclic reaction in the isomerization of 2,2′-diphenoquinones.

The diol (5) was prepared by a crossed Ullmann coupling of the appropriate iodides, protected as their isopropyl and




methyl ethers. After chromatographic separation of the desired biphenyl (11) the protecting groups were selectively cleaved with one equivalent of boron trichloride, the selectivity presumably resulting from the proximity of the two groups involved.

In an attempt to induce the isomerization of a *trans*-diphenoquinone to the *cis*-isomer, one of the most stable quinones (1c) was subjected to u.v. irradiation; because of its insolubility chloroform was used as the solvent. The product was the demethylated quinone (12), presumably formed by acid-catalysed hydrolysis, a mere trace of photochemically produced hydrochloric acid being sufficient for this reaction.[3]

Although the diphenoquinone (1c) is the major product of the ferricyanide oxidation of 3,4-dimethoxyphenol,[14] chromatography of the mother liquors produced 19% of the corresponding dibenzo[*d*,*f*][1,3]dioxepin (13). This is of interest as the first reported example of such an oxidation product from a phenol with only oxygen substituents.

## Experimental

General details are as given in Part 26.[3]

*General Procedure for Examination by F.T. N.m.r. of Unstable 2,2′-Diphenoquinones (Bicyclohexa-3,5-dien-1-ylidene-2,2′-diones).*—The diphenoquinones were prepared by oxidation of the corresponding biphenyl-2,2′-diols (10 mg) which was carried out by shaking the latter compounds vigorously in $CCl_4$ (1 ml) with potassium ferricyanide (5%)–sodium hydroxide (2%) (1 ml) for 10 s. The sample was rapidly filtered through tissue paper in a pipette directly into the n.m.r. tube. The examination was complete *ca.* 2.5 min after oxidation was commenced.

*5,5′-Dibenzyloxy-4,4′-di-t-butylbiphenyl-2,2′-diol.*—The literature yield [14] (48%) of 4-benzoyloxy-2-t-butylphenol was increased by the following procedure. To a stirred solution of t-butylhydroquinone (16.6 g) in pyridine (9 g) and $CH_2Cl_2$ (85 ml) was added benzoyl chloride (14.5 g) dropwise at a rate sufficient to sustain reflux; stirring was continued for a further 1 h. Dilute hydrochloric acid was added and the mixture was extracted with hexane. This extract was washed with water and evaporated to give the *benzoate* which was crystallized from hexane–$CH_2Cl_2$ (21 g), m.p. 110—117 °C (lit.,[15] 112—113 °C). A small sample was recrystallized and had m.p. 121—122 °C. A solution of the benzoate (2.7 g) in *N*,*N*-dimethylformamide (DMF) (13 ml) was stirred overnight

under nitrogen with benzyl bromide (1.9 g) and potassium carbonate (2.1 g). Water (26 ml) was added and the mixture was extracted with ether. This extract was dried ($MgSO_4$) and evaporated to give *5-benzoyloxy-2-benzyloxy-t-butylbenzene* (3 g), m.p. 100—102 °C, crystallized from hexane–ether (Found: C, 79.7; H, 6.4. $C_{24}H_{24}O_3$ requires C, 80.0; H, 6.7%); δ($CDCl_3$) 1.38 (Bu$^t$), 5.05 ($CH_2$), and 6.9—8.2 (13 ArH); $M^+$ 340. A solution of this material (1.4 g) in methanol (28 ml) was refluxed under nitrogen overnight with a solution of sodium hydroxide (1.4 g) in water (4 ml). After acidification the mixture was extracted with hexane. This was washed with aqueous sodium hydrogen carbonate until effervescence ceased, then with water. On evaporation 4-benzyloxy-3-t-butylphenol (0.85 g) was obtained as an oil (Found: C, 79.6; H, 7.7. Calc. for $C_{17}H_{20}O_2$: C, 79.7; H, 7.9%); δ($CCl_4$) 1.37 (Bu$^t$), 4.3 (OH), 5.03 ($CH_2$), 6.44—6.80 (3 ArH), and 7.31 (5 ArH); $M^+$ 256. A portion of this phenol (0.6 g) without purification was dissolved in hexane (90 ml) and shaken with potassium ferricyanide (3 g) and sodium hydroxide (1 g) in water (30 ml) for 1 min and the organic layer was separated. After standing overnight the solution was decanted from polymeric material (0.1 g) and filtered through Celite. The solution was evaporated and the residue crystallized from hexane–$CH_2Cl_2$ to give *2′,5,10′-tribenzyloxy-3′,4,9′-tri-t-butylspiro(cyclohexa-3,5-diene-1,6′-dibenzo*[d,f][1,3]*dioxepin)-2-one* (0.18 g), m.p. 172—176 °C. A small sample recrystallized from acetone-water had m.p. 178—181 °C (Found: C, 80.5; H, 7.2. $C_{51}H_{54}O_6$ requires C, 80.3; H, 7.1%); δ($CCl_4$) 1.32, 1.44 (2) (Bu$^t$), 4.70, 5.04 (2) ($OCH_2$), 5.38, 5.94 (vinyl H), 6.76, 6.94 (4 ArH), and 7.28—7.36 (15 ArH). A solution of this dioxepin (100 mg) in methanol (15 ml) was refluxed for 4 h with concentrated HCl (0.5 ml), then water (15 ml) was added and the mixture was extracted with hexane. This was washed with water and evaporated. The residue was dissolved in methanol and sodium borohydride was added until the solution was colourless. After acidification, addition of water and cooling, *5,5′-dibenzyloxy-4,4′-di-t-butylbiphenyl-2,2′-diol* (40 mg) crystallized, m.p. 82—85 °C. After purification on silica t.l.c. and crystallization from hexane, the m.p. was 186—189 °C (Found: C, 79.7; H, 7.5. $C_{34}H_{38}O_4$ requires C, 80.0; H, 7.5%); δ($CCl_4$) 1.41 (Bu$^t$), 4.93 ($OCH_2$), 5.1 (OH), 6.60, 6.87 (4 ArH), and 7.25—7.39 (10 ArH); $M^+$ 510.

*5-Methoxy-3′,4,5′-tri-t-butylbiphenyl-2,2′-diol*.—A sample of 5-isopropyloxy-2-methoxy-t-butylbenzene (5 g), prepared as described previously [1] and unpurified, was stirred in $CH_2Cl_2$ (50 ml) with silver trifluoroacetate (6.5 g) and iodine (6.3 g) for 0.5 h. The solution was filtered, washed with sodium thiosulphate solution, then with water, and evaporated. Purification through alumina gave *2-isopropyloxy-5-methoxy-4-t-butyliodobenzene* (6.3 g) as an oil (Found: C, 48.6; H, 6.0; I, 36.3. $C_{14}H_{21}IO_2$ requires C, 48.3; H, 6.1; I, 36.4%); δ($CCl_4$) 1.29 (Bu$^t$), 1.30 (d, 2 Me, *J* 6.0 Hz), 3.69 (OMe), 4.28 (sept., 1 H, *J* 6.0 Hz), and 6.62, 7.00 (2 ArH); $M^+$ 348. In a similar procedure 2,4-di-t-butylmethoxybenzene [16] (6.6 g) with silver trifluoroacetate (8.6 g) and iodine (8.4 g) gave, on crystallization from methanol, *2-methoxy-3,5-di-t-butyliodobenzene* (8.0 g), m.p. 39—42 °C (Found: C, 52.0; H, 6.7; I, 36.7. $C_{15}H_{23}IO$ requires C, 52.0; H, 6.7; I, 36.7%); δ($CCl_4$) 1.33, 1.25 (2 Bu$^t$), 3.68 (OMe), 7.02 (d, 1 H, *J* 3.0 Hz), and 7.34 (d, 1 H, *J* 3.0 Hz); $M^+$ 346. These iodides (2 g of the former and 3 g of the latter) were heated with treated [17] copper bronze (5 g) at 240 °C for 0.5 h. The products were extracted with $CHCl_3$ and the extract was filtered and evaporated. The residue was chromatographed on alumina to yield *2,2′-dimethoxy-3,3′,5,5′-tetra-t-butylbiphenyl* (0.3 g), m.p. 211—212 °C after crystallization from acetone (Found: C, 81.9; H, 10.8. $C_{30}H_{46}O_2$ requires C, 82.2; H, 10.5%); δ($CCl_4$) 1.30, 1.38 (4 Bu$^t$), 1.14 (2 OMe), and 7.08 (4 ArH); $M^+$ 438. This was identical with a sample prepared by subjecting 3,5-di-t-butyl-2-methoxyiodobenzene alone to the same Ullmann condensation. The second fraction eluted was *2′-isopropyloxy-2,5′-dimethoxy-3,4′,5-tri-t-butylbiphenyl* (0.37 g), an oil; δ($CCl_4$) 1.14 (d, 2 Me, *J* 6 Hz), 1.30, 1.38, 1.39 (Bu$^t$), 3.20, 3.72 (OMe), 4.20 (sept., CH, *J* 6 Hz), 6.72 (2 ArH), and 6.97, 7.06 (d, 2 ArH, *J* 2.5 Hz); $M^+$ 440. Without purification a portion of this biphenyl (0.17 g) in $CCl_4$ (1 ml) was cooled in an ice-bath and stirred with boron tribromide (3.7 ml of a 1% solution in $CH_2Cl_2$) and allowed to warm to 18 °C during 25 min. The solution was poured onto ice and extracted with ethyl acetate. This extract was washed with water and evaporated. Purification by t.l.c. gave the desired *biphenyl-2,2′-diol* (0.08 g) which crystallized from methanol, m.p. 79—80 °C (Found: C, 77.8; H, 9.3. $C_{25}H_{36}O_3$ requires C, 78.1; H, 9.4%); δ($CCl_4$) 1.27, 1.34, 1.40 (Bu$^t$), 3.76 (OMe), 4.6, 5.2 (OH), 6.54, 6.78 (ArH), 6.86 (d, 1 H, *J* 2.5 Hz), and 7.14 (d, 1 H, *J* 2.5 Hz); $M^+$ 384.

*2′,3′,4,5,9′,10′-Hexamethoxyspiro(cyclohexa-3,5-diene-1,6′-dibenzo*-[d,f][1,3]*dioxepin)-2-one* (13).—3,4-Dimethoxyphenol (13 g) was oxidized with alkaline potassium ferricyanide as described previously.[14] After filtration of the 2,2′-diphenoquinone (1c) the chloroform layer was washed with water, dried and evaporated. Chromatography of the residue on alumina and elution with hexane–chloroform (10 : 3) gave the *dioxepin* (2.5 g) as yellow needles, m.p. 191.5—192.5 °C, from methanol (Found: C, 63.1; H, 5.5. $C_{24}H_{24}O_9$ requires C, 63.15; H, 5.3%); δ($CDCl_3$) 3.64 (OMe), 3.81 (3 OMe), 3.88 (2 OMe), 5.34, 5.41 (olefinic H), 6.53 (2 ArH), and 6.83 (2 ArH); $\nu_{max.}$ ($CHCl_3$) 1 665 and 1 678 $cm^{-1}$; $M^+$ 456.

*2-(2-Hydroxy-4,5-dimethoxyphenyl)-5-methoxy-1,4-benzoquinone*.—A solution of 3,4-dimethoxyphenol (1.5 g) in methanol (25 ml) was stirred with aqueous ferric chloride (10%, 75 ml) for 1 h. The blue solution was filtered and the precipitate was dried, recrystallized from benzene–hexane, chromatographed on alumina, and finally recrystallized from benzene giving the *quinone* (170 mg), m.p. 189.5—190 °C (Found: C, 62.0; H, 5.1. $C_{15}H_{14}O_6$ requires C, 62.1; H, 4.9%); δ($CDCl_3$) 3.83 (OMe), 3.89 (2 OMe), 6.06, 6.57, 6.66, and 6.71.

*Photolysis of 4,4′,5,5′-Tetramethoxy-2,2′-diphenoquinone* (1c).—The quinone (100 mg) in chloroform (100 ml) was irradiated under nitrogen in a Hanovia reactor at 300 and 350 nm for 5 h. The solvent was removed under reduced pressure and the residue was chromatographed on a silica plate, developed in chloroform. Recrystallization of the only coloured band from benzene gave 2-(2-hydroxy-4,5-dimethoxyphenyl)-5-methoxy-1,4-benzoquinone (12), m.p. 186—187 °C, identical with the sample described above.

## Acknowledgement

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